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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,190	11/13/2001	Kazutoh Takesako	1422-0502P	6479

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 04/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/987,190	TAKESAKO ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/28/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-3,5 and 7-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~2/8/05~~ 2/28/05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment

1. Applicants amendment filed on 1/28/05 is acknowledged and entered.

Status of Claims

2. Claims 4 and 6 have been amended.

Claim 21 is canceled.

Claims 4 and 6 are under examination.

Claims 1-3, 5 and 7-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Information Disclosure Statement

3. The Information Disclosure Statement submitted on 2/28/05 is acknowledged and a signed copy is attached to this Office action.

Priority

4. Applicant states that the Examiner indicates that priority for the present claims is accorded that of the filing date of parent application 09/262,856, filed on March 4, 1999. However, the Examiner indicates that there is no support for an isolated nucleic acid in PCT/JP97/03041, filed August 29, 1997. Applicants respectfully disagree with the Examiner because a review of the relevant publication corresponding to PCT/JP97/03041 reveals that sequences recited in the present claims are fully supported by the specification as originally filed in PCT/JP97/O3041.

The Examiner disagrees with the applicant because applicant has not pointed to the sequence identification number or the figure of the claimed DNA sequence in the priority document PCT/JP97/0304I. Therefore, the priority for the present claims will be accorded as of the filing date of the Parent application 09/262,856 (U.S.Patent 6,333,164) filed on 3/4/1999 as

there is no support found for isolated nucleic acid in PCT/JP97/0304l, 8/29/1997. Applicant is encouraged to show the specific support for the claimed invention, i.e., nucleic acid in the priority document.

Claim Rejections - 35 USC 112, first paragraph maintained

5. The written description rejection of claims 4 and 6 under 35 U.5.C. 112, first paragraph is maintained as set forth in the previous Office action,

Claim 4 is drawn to an isolated nucleic acid encoding a fungal antigen comprising an antigenic protein having a vaccine activity or an allergen activity originating from Candida albicans, wherein said antigenic protein comprises the amino acid sequence as shown by SEQ ID NO: 2 in Sequence Listing and has a molecular weight of about 25,000 Daltons as determined by SDS-PAGE under reduced conditions.

Claim 6 is drawn to an isolated nucleic acid encoding a fungal antigen which originates from the genus Candida and has a molecular weight of about 25,000 Daltons and has a vaccine activity or an allergen activity, wherein said nucleic acid hybridizes to a nucleic acid which encodes a fungal antigen comprising an antigenic protein having a vaccine activity or an allergen activity originating from Candida albicans in 6X SSC, wherein l x SSC indicates 0.15 M NaCl, 0.015 M sodium citrate, and PH 7.0, containing 0.5% SDS, 0.1% bovine serum albumin (BSA), 0.1% polyvinyl pyrrolidone, 0.1% Ficoll 400, and 0.01% denatured salmon sperm DNA at 50^0C; followed by washing initially at 37^0C in 2X SSC containing 0.5%SDS and changing the SSC concentration to 0.lX SSC and the SSC temperature to 50^0C, wherein said antigenic protein comprises the amino acid sequence as shown by SEQ ID NO: 2 in Sequence Listing and has a molecular weight of about 25,000 Daltons as determined by SDS-PAGE under reduced conditions.

The claims 4 and 6 encompass an isolated nucleic acid encoding a fungal antigen comprising an antigenic protein comprising the amino acid sequence as shown by SEQ ID NO: 2 from *Candida albicans* and has a molecular weight of about 25,000 as determined by SDS-PAGE under reduced conditions and claim 6 recites any isolated DNA encoding a fungal antigen comprising an antigenic protein comprising the partial amino acid sequence as shown by SEQ ID NO: 2 from genus Candida which includes *Candida galli, Candida asparagi, Candida diospyri, Candida qinlingensis, C. tropicalis and C. glabrata* and *Candida albicans* etc which would hybridize thereto under moderate conditions to an isolated nucleic acid encoding a fungal antigen comprising an antigenic protein comprising the partial amino acid sequence as shown by SEQ ID NO: 2 from *Candida albicans.* Review of the present specification and the sequences of record for claimed isolated nucleic acid indicates that such an isolated nucleic acid has not been identified or described. Presently, in order to practice the invention as claimed the artisan must first obtain the claimed isolated nucleic acid encoding a fungal antigen comprising the amino acid sequence as shown by SEQ ID NO: 2 and has a molecular weight of

about 25,000 daltons. However, the present specification does not teach the structure of the claimed nucleic acid. Moreover, the specification fails to describe any other representative species (*Candida galli, Candida asparagi, Candida diospyri, Candida qinlingensis, C. tropicalis and C. glabrata*) of genus Candida by any identifying characteristics or properties other than the functionality of encoding fungal antigen. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants' arguments filed on 1/28/05 has been fully considered but they are not deemed to be persuasive.

Applicant states that the applicants have clarified the language of claims 4 and 6. Applicants pointed out that SEQ ID NO: 2 is 100% of the amino acid sequence that is encoded by the claimed nucleic acid, rather than SEQ ID NO: 2 being only a portion of the amino acid sequence that is encoded by the claimed nucleic acid may be obtained by affinity chromatography (see page 34) or ion exchange chromatography (see page 35). Also, at pages 40-41 of the specification it is explained that the information of the amino acid sequence can be used to isolate a nucleic acid by PCR. The particular DNA encoding the amino acid sequence of SEQ ID NO: 2 is not disclosed in the present specification, however, such disclosure is not necessary. Applicant cites In re Wallach, 71 U.S.P.Q.Zd 1939 at 1942 (Fed. Cir. 2004) to supports this rationale.

The examiner reviewed the specification pages 40-41 and understands that the protein SEQ.ID.NO: 2 is obtained from the Fungal cells, *Candida albicans*. However, the DNA sequence encoding said protein Lys Tyr Ser Leu Pro Glu Leu Asp Tyr Glu Phe Ser Ala Thr Glu Pro Tyr Ile Ser Gly Gln Ile Asn Glu Ile Xaa Tyr Thr Xaa Xaa. is not disclosed. Please note each application is reviewed on its merits. The DNA encoding the human urine proteins recited In re Wallach, 71 U.S.P.Q.Zd 1939 at 1942 (Fed. Cir. 2004) is a complete sequence and do not

encode any unknown Xaa amino acids. However, applicant is claiming a particular DNA that encodes a protein that contains unknown (Xaa) amino acids.

Applicant states that the claims have been amended to delete the limitation "partial" and therefore, the nucleic acid sequence encoding the amino acid sequence, SEQ.ID.NO: 2 is being claimed and the DNA being claimed is only as much as it corresponds to the amino acid sequence of SEQ ID NO: 2 and therefore the present inventors are in possession of the claimed invention..

The examiner disagrees with the applicant because the claimed nucleic acid encodes the amino acid sequence that contains an unknown Xaa amino acids. It is not clear to the examiner what nucleic acid is being claimed. Further, an isolated nucleic acid encoding a fungal antigen comprising an antigenic protein having a vaccine activity or an allergen activity originating from Candida albicans, wherein said antigenic protein comprises the amino acid sequence as shown by SEQ ID NO: 2 as claimed is broader than the nucleic acid encoding the amino acid sequence and the specification lacks support for the claimed invention. Similarly, broadly claimed "nucleic acid, which hybridizes to a nucleic acid which encodes a fungal antigen comprising an antigenic protein having a vaccine activity or an allergen activity originating from *Candida albicans* in 6X SSC, ---- to 50^0C" is not disclosed. Further, isolated nucleic acid that hybridizes to a nucleic acid would h encode a fungal antigen has not been disclosed by the present specification. Therefore, the rejection is maintained.

6 The enablement rejection under 35 U.5.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained as set forth in the previous Office action.

The specification (pages 96-98) describes as a part of invention *C.albicans* 25kD protein in a solubilized fraction by using solublizer from the insoluble fractions from fungal cells of which cell wall has substantially removed or partially purified and comprises the N-terminal amino acid sequence as shown by SEQ ID NO: 2. However, the specification fails to disclose the same *C.albicans* 25kD protein comprising the amino acid sequence SEQ.ID.NO:

2,KYSLPELDYEFSATEPYISGQINEIXYTXX Or a cDNA sequence (having start and stop codons) from *C.albicans* that encodes a fungal antigen comprising the amino acid sequence as shown by SEQ ID NO: 2, KYSLPELDYEFSATEPYISGQINEIXYTXX or the claimed protein from other representative species of *Candida galli, Candida asparagi, Candida diospyri, Candida qinlingensis, C. tropicalis and C. glabrata.* The specification fails to provide any detail on an isolated nucleic acid encoding 25kD fungal antigen comprising the partial amino acid sequence SEQ.ID.NO: 2. In the instant case, the claimed embodiments of the polynucleotide sequence are needed to make use of the invention as claimed. To decide whether a specification is enabling, it is to be determined whether the specification discloses sufficient guidelines for successful making and using of the claimed invention without undue experimentation.

Applicants' arguments filed on 1/28/05 has been fully considered but they are not deemed to be persuasive.

Applicant states that the present specification explains that the information of the amino acid sequence (for instance, that of SEQ ID NO: 2) can be used to prepare isolated nucleic acids by PCR. Additionally, it is explained (see pages 40-41) that a CDNA library can be prepared from cells expressing a desired antigenic protein. Next, the PCR is carried out with genomic DNA for the cells expressing the antigenic protein as a template, by using an oligonucleotide usable as a primer (which is designed based upon a nucleotide sequence)extrapolated from the amino acid sequence as well as a suitable primer pair. A DNA encoding the desired antigenlc protein can then be selected from the cDNA library by hybridization using a DNA fragment obtained by this PCR.

The examiner disagrees with the applicant because while general techniques of cloning and expression of proteins using specific primer sequences are known in the art, using incomplete amino acid sequence to obtain a nucleic acid by PCR is not routine in the art. In addition, Adra et al (PNAS, 1997, Vol.94, pp. 4279-4284) teach that over expression of RhoGDI γ protein in baby hamster kidney cells caused the cells to round up with loss of stress fibers and transfection of GST-RhoGDI γ fusion cDNA into bacteria produced insoluble protein and is difficult to purify. Thus, predictability of protein is not necessarily contingent on nucleic acid and mRNA expression due to the multitude of homeostatic factors affecting transcription and

translation. Therefore, one of skill in the art would not be able to predict the nucleic acid encoding the amino acid sequence, SEQ ID NO: 16 having unknown amino acids. As stated above, the specification fails to provide sufficient guidelines for a skilled artisan to have practiced the invention as claimed without undue experimentation because the specification does not provide sufficient guidance for making and using the invention as claimed.

Claim Rejections - 35 USC 102 maintained

7. The rejection of claims 4 and 6 under 35 U.S.C. 102(b) as being anticipated by Buckley et al, Infect Immun. 1982 September; 37 (3): 1209–1217 is maintained as set forth in the previous Office action,

Buckley et al disclose isolated nucleic acid, DNA (see abstract) from C.albicans cultures that were grown in the presence of ['4C] Uralic for at least six mass doublings (0.5, uCi/ml with 50 ug/ml of carrier uraci). Samples (0.5 ml) were precipitated in 5 ml of 10% trichloroacetic acid and were extracted with alkali by the method of Hatzfield .The residue from alkali treatment could be solubilized totally by hydrolysis in 10% trichloroacetic acid. (Page 1210, left column, last paragraph) Thus the solubilized sample contains isolated nucleic acid, which inherently encodes a fungal antigen having the recited properties. Characteristics such as molecular weight, the partial amino acid sequence are inherent in the preparation of isolated DNA extract, such a DNA would hybridize to isolated nucleic acid as claimed in claim 6. Thus the prior art anticipated the claimed invention.

Since the Office does not have the facilities for examining and comparing applicants' product with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicants' arguments filed on 1/28/05 has been fully considered but they are not deemed to be persuasive.

Applicant states that the nucleic acid disclosed in Buckley is prepared by precipitating a sample culture medium of *C. albicans* is with trichloroacetic acid, extracting the precipitates obtained with an alkali, and solubilizing the residue with trichloroacetic acid. In such simple treatments is not possible to obtain an isolated nucleic acid in which polysaccharides and

proteins contained in the cells are removed. In fact, there is no description in Buckley that a nucleic acid (DNA) could be isolated by the above-mentioned method.

The examiner disagrees with the applicant because in the absence of the structure of the claimed nucleic acid, the DNA disclosed in the prior art reads on the claimed invention because the preparation contains nucleic acid encoding fungal antigen. Further, applicant is not claiming the product by a process. Therefore, the prior art DNA reads on the claimed invention.

Further, applicant states, the DNA described in Buckley is a mixture of a nucleic acid and does not encode a fungal antigen as claimed the present application and the disclosed nucleic acid is not capable of hybridizing to a nucleic acid encoding the fungal antigen as recited in the claim. Therefore, the DNA described in Buckley does not correspond to the isolated nucleic acid' as recited in the present application.

The examiner rejected the claimed invention because open-ended claim language "comprising" in the claims does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See *Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App.1948).* Therefore, the prior art mixture of nucleic acid encoding fungal antigens read on the claimed invention. In the absence of structural characteristics of the claimed nucleic acid, the DNA described in Buckley is capable of hybridizing to a nucleic acid encoding the fungal antigen.

8. The rejection of claims 4 and 6 under 35 U.S.C. 102 (a) as being anticipated by Rhei et al Database GenEmbl, Acession number AF031478 (Biochim. Biophys. Acta 1426 (3), 409-419 (1999) is maintained as set forth in the previous Office action.

Rhie et al 1999 discloses an isolated nucleic acid molecule (see page 412 in Biochim. Biophys. Acta 1999) encoding a fungal antigen (see figure 5 in Biochim. Biophys. Acta 1999) from

Candida albicans . As this protein comprises more than 6 amino acids it is an antigenic protein because peptides having 5-6 amino acids induce an immune response and are well accepted as antigens in the art of immunology. As this protein is isolated from fungus Candida albicans, the properties of a fungal antigen such as allergen activity are considered as an inherent property of the disclosed antigen. The N-terminal amino acid sequence alignment showed (see the sequence alignment) that the claimed protein encoded by nucleic acid and the prior art nucleic acid encoding the protein is identical. The gene sod2 encoding manganese-containing super oxide dismutase has been cloned using a product obtained from polymerase chain reaction. Sequence analysis of the sod2 predicted a manganese-containing super oxide dismutase that contains 234 amino acid residues with a molecular mass of 26173 daltons, and thus read on the claimed invention. The deduced N-terminal 34 amino acid residues serve as a signal peptide for mitochondrial translocation. Northern analysis with a probe derived from the cloned sod2 revealed a 0.94-kb band, which corresponds approximately to the expected size of mRNA deduced from sod2 and is expected to hybridize to the claimed nucleic acid. Thus the disclosed nucleic acid sequence read on claim 6 because it contains a partial amino acid sequence that is 100%identical to the partial amino acid sequence of the claimed protein and is encoded by the nucleic acid. The disclosed nucleic acid is 100% identical to the nucleic acid sequence of the claimed isolated nucleic acid and therefore would hybridize to the claimed nucleic acid as recited in claim 6. Further the nucleic acid is originated from genus Candida. The prior art anticipated the claimed invention.

9. The rejection of claims 4 and 6 under 35 U.S.C. 102 (e) as being anticipated by

Weinstock et al U.S.Patent 6,747,137 is maintained as set forth in the previous Office action.

Weinstock et al disclose an isolated nucleic acid molecule (SEQ.iD.NO: 3165 in patent) encoding a Candida fungal antigen (see SEQ.ID.NO: 17718 in the Patent). The disclosed protein comprises the partial amino acid sequence SEQ.ID.NO: 2 and is 100%identical to the protein encoded by the claimed nucleic acid as shown below (Qy is the partial amino acid sequence of SEQ.ID.NO: 2 and Db is the prior art nucleic acid, SEQ.ID.NO: 3615) in the sequence alignment. As this protein comprises more than 6 amino acids it is an antigenic protein because peptides having 5-6 amino acids induce an immune response and are well accepted as antigens in the art of immunology. The disclosed protein is isolated from fungus Candida albicans, therefore, the properties of a fungal antigen such as allergen activity are considered as an inherent property of the disclosed antigen. The N-terminal amino acid sequence alignment showed (see the sequence alignment) that the claimed protein encoded by nucleic acid and the prior art nucleic acid encoding the protein is identical.

The prior art nucleic acid sequence encoding a fungal antigen reads on claimed protein having a molecular weight of about 25000 doltons because the disclosed protein has 229 amino acids (each amino acid is approximately 110 daltons). The disclosed nucleic acid is 100% identical to the nucleic acid sequence of the claimed isolated nucleic acid and therefore would hybridize to the claimed nucleic acid as recited in claim 6. Further the nucleic acid is originated from genus Candida. The prior art anticipated the claimed invention.

Applicants' arguments filed on 1/28/05 has been fully considered but they are not

deemed to be persuasive.

Applicant states that the Rhei reference/Weinstock reference is not prior art because they are published 1999 and the current application gets priority to PCT/JP97/O3041, August 29, 1997.

The examiner has clearly stated why this application does not get priority as of the filing date of 8/29/97 the PCT/JP97/O3041 in paragraph # 4 under priority. Since the application does not get priority as of 1997, the prior art of record anticipated the claimed invention.

Remarks

10. No claims are allowed.

Conclusion

11. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

Information regarding the status of an application may be obtained from the Patent Application information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message

may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Padma Baskar Ph.D.